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Public Health Service Progress Report

on the

Poliomyelitis Vaccination Program

January 24, 1956

PUBLIC HEALTH SERVICE PROGRESS REPORT ON THE POLIOMYELITIS VACCINATION PROGRAM

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PUBLIC HEALTH SERVICE PROGRESS REPORT ON THE POLIOMYELITIS VACCINATION PROGRAM

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INTRODUCTION

The purpose of this report is to review the progress of the poliomyelitis vaccination program since April 12, 1955. Because events prior to July 25, 1955, have been discussed in detail in previous reports 1, 2, 3, they are only briefly summarized here. Primarily, this report deals with progress in the production, clearance, distribution, and use of poliomyelitis vaccine, and special attention is given to the present status of the program.

The two major goals of the Department of Health, Education, and Welfare with respect to the poliomyelitis vaccine program have been: 1, to ensure safety and effectiveness of the vaccine produced; and 2, to help obtain equitable distribution and use of the limited supply of vaccine available.

The report is keyed to these goals, and is presented in three main parts.

Part I reviews the steps that have played important roles in determining the safety and effectiveness of the vaccine.

Part II is devoted to activities which, moving forward simultaneously on another front, have had a significant effect on the supply, distribution, and use of poliomyelitis vaccine.

Part III summarizes the current status of the program from the standpoints of safety, effectiveness, supply, distribution, and use.

Part I

SAFETY AND EFFECTIVENESS

Licensing of Producers of Poliomyelitis Vaccine

As a direct result of the field trials with Salk vaccine carried out by the National Foundation for Infantile Paralysis, the Public Health Service

Laboratory of Biologics Control[1] on April 12, 1955, issued official minimum requirements for poliomyelitis vaccine (4). Also, on advice of a group of special consultants, it accepted the evidence available as warranting licensing of six manufacturers of the vaccine. Consequently, on the same day, upon the Surgeon General's recommendation, the Secretary of Health, Education, and Welfare issued licenses to the following companies which were producing vaccine and had filed licenses applications: Parke, Davis & Company; Eli Lilly Company; Wyeth Laboratories, Inc.; Cutter Laboratories; Pitman-Moore Company; and Sharp & Dohme.

Stocks of vaccine, tested by manufacturers in anticipation of licensing, were already on hand. Samples of the vaccine had been submitted to the National Institutes of Health, which had tested one or more lots of each manufacturer prior to licensing. After review by the Laboratory of Biologics Control of submitted records of manufacturing and testing (protocols), a number of lots of vaccine were released for use, thus enabling the national program of poliomyelitis vaccination to get underway within two days after the licenses were issued.

Testing and Clearance of the Vaccine

Suspension and Resumption of the Vaccination Program

On April 26 five cases of paralytic poliomyelitis were reported in vaccinees who had been injected with vaccine produced by the Cutter Laboratories. The following day, this Company was requested to withdraw its product, and thereupon notified its distributors to recover all vaccine. Experts from the National Institutes of Health were sent to Cutter Laboratories to examine the records and the physical plant, and efforts were begun to test Cutter products by enlisting the aid of 16 cooperating laboratories.

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[1]Now the Division of Biologics Standards, which was established on June 9, 1955. (See page 5 for fuller explanation.)

In addition, upon recognition that cases of poliomyelitis were occurring in association with vaccine manufactured by the Cutter Laboratories, the Surgeon General immediately (April 28) established the National Poliomyelitis Surveillance Program. The purpose of the program was to provide a clearing house for the collection, consolidation, and dissemination of all pertinent epidemiologic information regarding the occurrence of poliomyelitis in vaccinated and unvaccinated persons. Operation of this program is discussed later in this report.

By April 30, seventeen cases of paralytic poliomyelitis had been reported among children injected with Cutter vaccine. Upon recommendation of a Special Committee of Experts, the Surgeon General on May 8 recommended suspension of vaccination programs until each manufacturing plant had been visited and its records and procedures inspected. As a result of visits to the Parks, Davis and the Eli Lilly plants, vaccine produced by these two companies was recleared for use. Wyeth and Pitman-Moore vaccine was subsequently recleared also. The Sharp and Dohme company has not yet presented any vaccine for release.

The Cutter Report. A prolonged and intensive study was made of the Cutter manufacturing plant, its protocols and records, and the completed product in an effort to determine the cause of the Cutter problem. The report of the study was issued by the Surgeon General on August 25, 1955 (5).

Reappraisal of Production Procedures and Testing Methods

By May 15, a total of 54 cases of paralytic poliomyelitis associated with Cutter vaccine had been reported. The Public Health Service decided that advice from the most experienced workers in the poliomyelitis field, based on a continuing review of production procedures and testing methods, was needed.

The Technical Committee on Poliomyelitis Vaccine. The Technical Committee on Poliomyelitis Vaccine (3) was appointed by the Surgeon General on May 23, 1955. This Committee has performed the following functions: 1, reviewing production and testing data on lots of vaccine submitted by manufacturers; 2, advising on

the release of such vaccine; 3, studying the details of manufacturing and testing procedure; 4, recommending requirements for production and testing which assure uniformly safe and potent vaccine; and 5, developing a collaborative research program which would continue to insure a sound basis of safe and effective manufacture of the vaccine.

Through repeated meetings and close cooperation among the manufacturers, the Technical Committee on Poliomyelitis Vaccine, and the Public Health Service staff of scientists, it has been possible to identify and develop corrective measures for a number of technical problems affecting consistent production of safe vaccine. These problems are discussed in the Committee's Interim Report (6), which includes the following statements:

"In summary, the Committee is of the opinion that the principal factors which were involved in manufacturing difficulties have been identified and corrective measures have been taken.

"Among these factors is the absolute need for removal of particles within which virus may be protected from inactivation by formaldehyde. Provisions have been made to ensure as far as possible the removal of such protected particles by suitably spaced filtration procedures.

"In addition, the safety test program has been strengthened by improved sampling procedures in the tissue culture tests and by increasing the sensitivity of the monkey safety tests. These measures, together with continuous review of plant production records, assure the safety of released vaccine and should make possible an increased availability of vaccine."

Throughout this period of intensive study, research leading to improvements and refinements in the vaccine has been emphasized. As the investigations proceeded and new information became available, the Public Health Service Minimum Requirements, governing poliomyelitis vaccine, have been amended accordingly. The principal changes involve improved filtration and more sensitive monkey tests.

Amendments to the Minimum Requirements. - Since the Minimum Requirements were first issued on April 12, 1955, they have been amended several times. Briefly, the subject of each may be stated as follows:

The first amendment to the Minimum Requirements, which was issued on April 19 (7), was concerned with a technical interpretation of the potency requirements. The second amendment, issued on May 26 (8), imposed more rigid methods of safety testing.

The adoption of these amendments and their application to the product enabled the vaccination program to continue. However, these changes in testing procedures served to retard temporarily the flow of vaccine. The tests now required larger volumes of material, thus tying up much of the personnel and resources which had previously been employed in the production of vaccine.

Continued investigation by the Technical Committee for Poliomyelitis Vaccine, the Division of Biologics Standards, various cooperating laboratories, and industry, led to the issue of Amendments 3 and 4 to the Minimum Requirements.

Amendment 3 (9) is concerned with a new monkey test evolved through the cooperation of various laboratories with the Division of Biologics Standards.

Amendment 4 (10) is concerned with the filtration steps designed to remove particulate materials from single strain pools prior to and during the process of inactivation and with the use of supplementary inactivation processes.

Amendment 4 also introduced modification of the monkey test, which emerged from experience since its introduction on September 10.

Establishment of the Division of Biologics Standards

Programs within the Division. The Division of Biologics Standards was established on June 9, 1955, as a component part of the National Institutes of Health to further expand and strengthen the Service's resources for controlling the safety of biologics products. Functions previously performed by the Laboratory of Biologics Control are included among the responsibilities of this new Division.

One of its first duties was to detail technical representatives to serve as liaison between the Public Health Service and each manufacturing concern. The resulting continuous interchange of information between industry and the controlling agency has been most helpful. Continuous surveillance of each manufacturing process ensures knowledge of inconsistency of performance should it occur. Heretofore, this had not been possible. A practical testing program has been instituted which is served by 5 tissue culture teams and is capable of testing all samples of vaccine submitted. In addition, a unit capable of performing monkey safety tests on a great proportion of vaccine samples submitted is in operation.

Cooperative Programs. Much of the research being carried out at the present time is based on the combined efforts of the Technical Committee for Poliomyelitis Vaccine, the manufacturing industry, and the Division of Biologics Standards. Problems under study include: methods of purifying vaccines, comparison of methods and techniques of tissue culture safety tests, the study of improved methods of employing monkey safety tests, and simian (wild) viruses and their relation to vaccine production and testing. Considerable effort has been expended in an attempt to improve the manufacturing methods employed in the various firms. A large scale effort is being made to discover a suitable strain of Type I virus as a substitute for the Mahoney strain. This is a most complex problem, with many diverse aspects such as inactivation, pathogenicity, potency and many related problems. The interim Report of the Technical Committee on Poliomyelitis Vaccine (Appendix F) summarizes the present status of this problem from a technical viewpoint.

Other Activities Concerned with Poliomyelitis Vaccine. The National Institutes of Health, in conjunction with the Technical Committee and representatives of the Surgeons General of the Army and Navy, have drafted the Minimum

Requirements for the manufacture of poliomyelitis vaccine into regulations governing manufacture of this product. In addition, the National Institutes of Health have been concerned with a review of the Biologics Control Act of 1902 with a view toward strengthening and modernizing control of the safety, purity, and potency of biologic products.

Surveillance of the Disease and Field Evaluation of the Safety and Effectiveness of the Poliomyelitis Vaccine

The National Poliomyelitis Surveillance Program, with headquarters at the Public Health Service Communicable Disease Center in Atlanta, Georgia, has proceeded concurrently with activities already described. This program, by following epidemiologically the experience of vaccinated and nonvaccinated children, has provided a double check on the success of corrective procedures developed by the virologists. In addition, it has demonstrated the effectiveness of the vaccine (11).

Epidemiologic Observations on Vaccine Safety

Poliomyelitis in Cutter Vaccinated Children and their Contacts. - The first concern of the Poliomyelitis Surveillance Unit was to evaluate the significance of the cases of poliomyelitis which were occurring among Cutter vaccinated children and their contacts. Upon study, certain characteristics became evident: 1, a concentration in certain geographic areas; 2, the association with particular lots of vaccine; 3, the grouping of the onset of most of the cases with appropriate incubation periods following inoculation; and 4, the correlation between the site of inoculation and the site of first paralysis in a majority of the vaccinated cases. Because of these characteristics, it was concluded that the development of the disease in some of these patients was the result of the presence, in infective amounts, of live poliomyelitis virus in some distribution lots of Cutter vaccine. Laboratory studies have since supported this conclusion.

Experience with Lots of Vaccine Since Revision of Testing Standards. - Since the revision of safety standards in May 1955, there has been no epidemiologic

evidence that any lot of vaccine of any manufacturer has been unsafe. Since May 13, all lots of vaccine have been released under revised safety standards. Epidemiologic surveillance for possible untoward incidents has been constantly maintained. All States and Territories report on a weekly basis cases of poliomyelitis which occur among vaccinated children. These are tabulated by lot number so that individual cases associated with the same lot but occurring in different States will be promptly recognized. Special attention is directed toward cases which occur at an interval of 4 to 14 days after inoculation and to paralytic cases showing first paralysis at the site of inoculation. The essential data on each vaccinated case are made available to health authorities.

The cases of poliomyelitis that have been reported among vaccinated persons since the first of July have shown certain distinctive characteristics. Over three-fourths have been reported as non-paralytic. Most have occurred more than 30 days after vaccination. Those few occurring in the interval 4 to 14 days did not exceed the normal expectancy of coincidence. Among the relatively infrequent paralytic cases, instances with first paralysis occurring within this interval at the site of inoculation have been conspicuously rare. Thus, from an epidemiologic viewpoint, there is no evidence that use of vaccine has caused poliomyelitis since the adoption of the new safety standards.

Measurement of the Effectiveness of Vaccine

Special Studies. - Preliminary reports indicate encouraging results regarding the effectiveness of the poliomyelitis vaccine, as demonstrated by experience from at least one injection. The restriction of inoculations to first and second grade school children during the spring and summer of 1955 provided a unique opportunity for special studies to evaluate effectiveness. Approximately 20 States are conducting such investigations. Preliminary reports have been received from 11 States and one city for inclusion in the two tables below. The

size of the study population and the number of cases by paralytic status are shown for each area in table 1. These data are used to calculate attack rates as shown in table 2.

Table 1

Summary of Special Studies Reported from 12 Areas
(Preliminary Reports Received through November 1, 1955)

Area	Age Group Studied	Period Studied		Vaccinated			Unvaccinated		
		From	To	Population	P	NP	Population	P	NP
California	6 to 8	6-15	10-15	395,000	13	47	431,000	43	45
Connecticut	5 to 9	1- 1	10-22	106,120	6	38	89,400	18	59
Florida	5 to 9	4-15	10-21	149,664	2	23	224,507	11	25
Georgia	6 to 11	4-16	10-23	174,200	6	6	262,400	20	19
Illinois	6 to 9	4-18	9-15	357,000	5	45	326,000	34	80
Maryland	5 to 9	4-12	10- 8	112,000	4		158,000	27	
Minnesota	6 to 9	5-20	10-28	112,115	3	21	33,259	10	12
N. Y. City	6 to 7	6- 1	10-21	166,000	9	13	87,000	19	32
N. Y. State	6 to 10	5-21	10-21	448,569	18	128	282,000	59	111
N. Carolina	5 to 9	4-12	10-21	196,466	4	19	232,133	26	58
Oregon	7 to 9	5-22	8-23	47,852	1	2	46,188	7	4
Washington	5 to 9	5-15	10-14	69,123	4	1	190,179	40	20
Total				2,334,109	75	343	2,362,066	313	465

P - Paralytic

NP - Non-paralytic

Table 2

Summary of Special Studies Reported from 12 Areas
Attack Rates by Paralytic Status among Vaccinated and Unvaccinated Children

(Preliminary Reports Received through November 1, 1955)

Area	Paralytic Rate per 100,000		Non-Paralytic Rate per 100,000	
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated
California	3.3	10.0	11.9	10.4
Connecticut	5.7	20.1	35.8	66.0
Florida	1.3	4.9	15.4	11.1
Georgia	3.4	7.6	3.4	7.2
Illinois	1.4	10.4	12.6	24.5
Maryland	3.6	17.1	-	-
Minnesota	2.7	30.1	18.7	36.1
New York City	5.4	21.8	7.8	36.8
New York State	4.0	20.9	28.5	39.4
North Carolina	2.0	10.8	9.7	25.0
Oregon	2.1	15.2	4.2	8.7
Washington	5.8	21.0	1.4	10.5
TOTALS	3.2	13.2	14.7	19.7

As shown in the second table, there is a marked difference between the attack rates for the vaccinated and unvaccinated groups. For paralytic cases, the rates are from two to more than five times greater in the unvaccinated than in the vaccinated groups. The total paralytic rate for the 12 areas combined was 4 times greater in the unvaccinated than the vaccinated group. For the non-paralytic cases, no differences were observed in some States, and rates in others for the unvaccinated were two or more times greater.

When final data--giving more accurate classification of cases--are available, some changes in the precise rates may be anticipated. It seems doubtful, however, that there will be a major departure from the favorable trends already noted.

Age Distribution Study

Confirmation of these preliminary findings has been obtained from a study of the pattern of the age distribution of cases of poliomyelitis reported this year from 33 States. Since it is known that the age-specific attack rates for poliomyelitis followed a relatively continuous distribution curve, and since use of poliomyelitis vaccine had been restricted almost solely to first and second grade children representing mostly 7 and 8 year olds, a discontinuity should appear in the age distribution this year if the vaccine were effective.

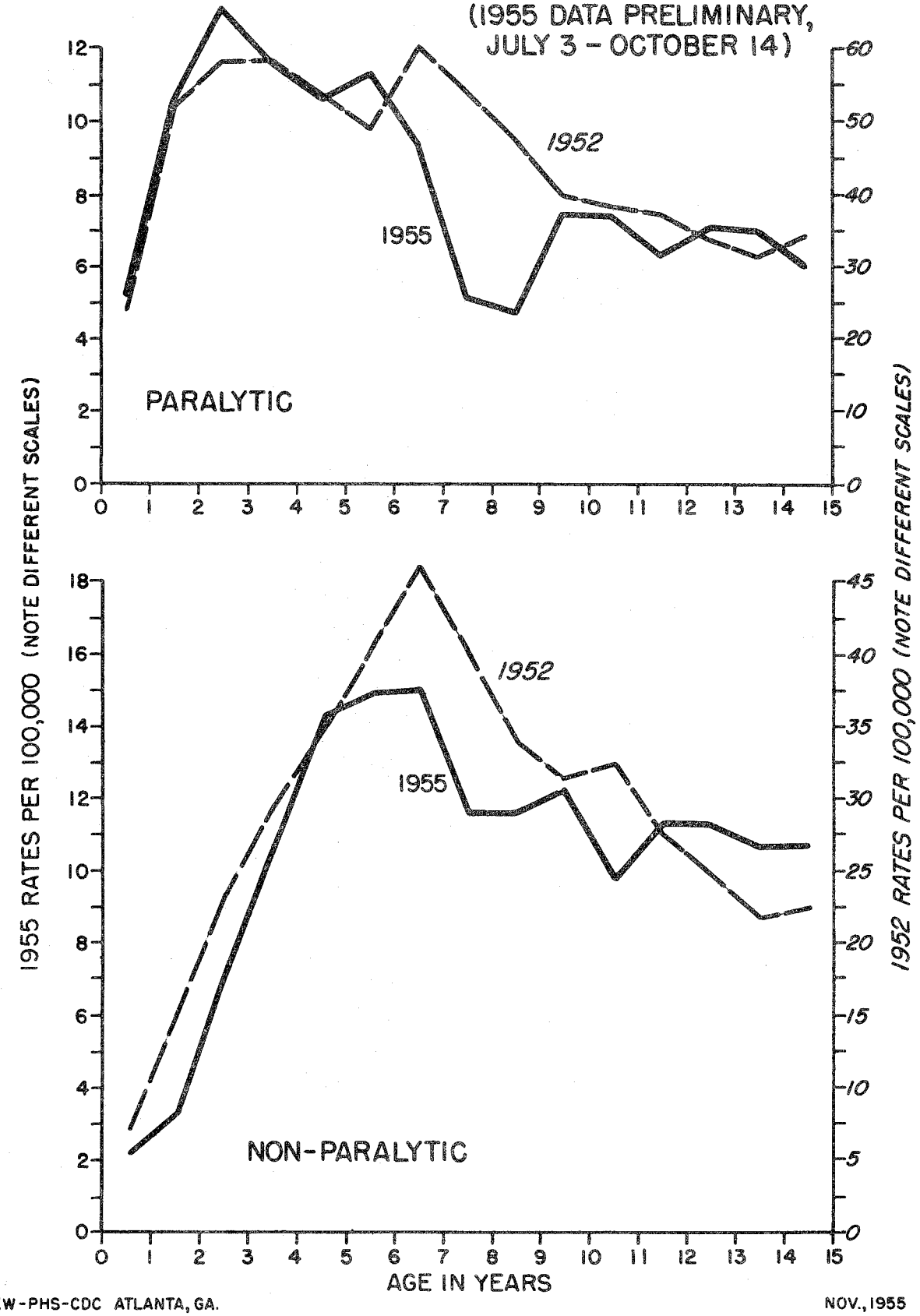
Chart 1 shows curves describing paralytic poliomyelitis for 1952 and 1955. The absolute level of the rates for the two years differs because of the greater severity of the epidemic in 1952 compared to 1955 and because data for the full calendar year are included for 1952 and data only for the period July 3 through October 14 are included for 1955. The two curves have been superimposed by a simple arithmetic transposition. The two rate scales are clearly shown.

The two distribution curves for paralytic cases are similar with one major exception, namely a relatively sharp lowering of the rates for ages 7 and 8 in 1955. Discontinuity in the age distribution curve is limited to the ages in which poliomyelitis vaccine was widely used this year. This constitutes independent evidence of the effectiveness of the vaccine against paralytic poliomyelitis.

In the lower half of the attached figure are shown age distribution curves for non-paralytic cases in 1952 and 1955. The same type of transposition factor

POLIOMYELITIS AGE-SPECIFIC ATTACK RATES IN 1955 (33 States) and 1952 (21 States)

(1955 DATA PRELIMINARY, JULY 3 – OCTOBER 14)



DHEW-PHS-CDC ATLANTA, GA.

NOV., 1955

has been used to superimpose the curves. No sharp discontinuity is discerned that can be clearly attributed to an effect of the vaccine on non-paralytic cases.

This evidence pointing to effectiveness of the vaccine in the vaccinated age group is substantiated by data on hospital admissions reported to the National Foundation for Infantile Paralysis for 1954 and 1955.

Thus, the epidemiological field studies conducted by the Poliomyelitis Surveillance Unit of the Public Health Service, working co-operatively with State medical and public health organizations throughout the poliomyelitis season, support the laboratory findings that the vaccine is safe and effective.

Part II

SUPPLY, DISTRIBUTION AND USE OF POLIOMYELITIS VACCINE

With announcement of the successful results of the 1954 field trials of Salk poliomyelitis vaccine, attention was immediately directed toward questions of supply, distribution, and use.

Supply of Vaccine Limited

Large-scale production of any new biologic product presents initial technical problems which can be solved only through experience. The problems inherent in the production of Salk vaccine are among the most complex in the field of large-scale biologic preparations. Hence, it was recognized that--even under the most favorable circumstances--demand for the vaccine would probably exceed the supply for a number of months.

On April 14, the President directed the Secretary of the Department of Health, Education, and Welfare to survey and report to him on the best means of assuring an equitable distribution of the Salk poliomyelitis vaccine. This report was submitted to the President on May 16, 1955 (1).[2] A follow-up report, supplemental to the original, was submitted on July 25, 1955.

Development of the Plan for Equitable Distribution of Vaccine, to Take Effect Upon Completion of National Foundation for Infantile Paralysis Program

Program of the National Foundation for Infantile Paralysis

In October 1954, the Foundation negotiated contracts with vaccine manufacturers for enough material to inoculate 9,000,000 children, provided the field trial

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[2] The many factors limiting the supply of vaccine available and the difficulties of estimating future production schedules were discussed in the May 16 report to the President (1). Moreover, during the early summer months, the problem was further complicated by the necessity for reappraisal of production and testing methods--referred to in Part I of this report.

indicated that the vaccine was effective. After consultation with a committee composed of representatives of the State and Territorial Health Officers Association, epidemiologists, and other health experts, it was decided to use this vaccine for first and second grade children. Subsequently, the Foundation decided to limit its purchase of vaccine to 18,000,000 cc. - enough for two injections for all first and second grade children, and for all participants in the field trials who had received placebo injections. In addition, children who had received vaccine in the 1954 field trials were to be given a booster injection. July 1, 1955, had been set as the goal for completion of this program.

The first objective of the Federal Government after success of the field trials was announced on April 12, 1955 - was to help assure rapid completion of the National Foundation's program. Because of production and testing problems referred to earlier in this report, this schedule was greatly delayed. However, as vaccine has been released, needs for the Foundation's program are being given priority until they are fully satisfied. From April 12 to late July, practically all vaccine released was shipped to the National Foundation for Infantile Paralysis to carry out its program. (During this period, only 563,000 cc. of vaccine were released for general sale - all prior to May 1.) Vaccine first became available for broader use on July 30. Since that time, the Foundation's orders have continued to be filled prior to allocation of vaccine for other purposes. As of December 31, 1955, approximately 13½ million cc. of vaccine had been released to the National Foundation.

National Advisory Committee on Poliomyelitis Vaccine

As one of the first steps in considering the problem of distributing the vaccine on an equitable basis, a National Advisory Committee on Poliomyelitis Vaccine was appointed. The functions of the Committee were to make recommendations to the Department regarding: 1, the best means of assuring an equitable distribution of the vaccine; 2, the age groups which should be given priority

to receive the vaccine because of their greater susceptibility to poliomyelitis; and 3, other broad problems which relate to the distribution and use of the vaccine.

The Committee is composed of representatives of the medical and pharmaceutical professions, the public health administration field, and the general public. The present membership of the Committee and the organizations represented are as follows:

Chairman: Dr. Chester Scott Keefer
Massachusetts Memorial Hospital
Boston, Massachusetts

Executive Secretary: Dr. Russell E. Teague, Chief
Poliomyelitis Vaccine Activity, Public Health Service

Members: Dr. Daniel Bergsma
State Commissioner of Health
State Department of Health
Trenton 7, New Jersey

Dr. George M. Uhl
Health Officer
City Health Department
Los Angeles, California

Dr. Malcolm Phelps
American Academy of General Practice
El Reno, Oklahoma

Dr. Philip S. Barba
American Academy of Pediatrics
5919 Green Street
Germantown, Pennsylvania

Mrs. Rollin Brown, President
National Congress of Parents and Teachers Association
700 North Rush Street
Chicago, Illinois

Mrs. Charles L. Williams, President
National Congress of Colored Parents and Teachers Association
1200 N. W. 6th Avenue
Miami, Florida

Dr. Robert P. Fischelis
Executive Secretary
American Pharmaceutical Association
2215 Constitution Avenue
Washington, D. C.

Mr. Frank W. Moudry
National Association of Retail Druggists
5th and St. Peter
St. Paul, Minnesota

Dr. Julian P. Price
Trustee of American Medical Association
117 W. Cheves Street
Florence, South Carolina

The secretariat to the Committee is made up of staff of the Public Health Service, which also serves as the administrative unit in connection with interstate distribution activities.

On May 2, 1955, the Committee held its first meeting. As the first order of business, the Committee endorsed the development and establishment of a voluntary system of vaccine distribution and recommended that children aged 5 through 9 be given the first priority to receive the vaccine. This Department concurred in these recommendations.

Interstate Plan for Distribution of Poliomyelitis Vaccine

Following the May 2 action of the National Advisory Committee on Poliomyelitis Vaccine, the Public Health Service continued in the development of a plan for the distribution and use of poliomyelitis vaccine.

Consultation with Many Groups and Agencies - In formulating plans, the Public Health Service consulted extensively with the vaccine manufacturers, representatives of the pharmaceutical and drug industries, the medical and public health professions, and the Conference of State Governors. Advice was sought also from organizations representing the consumer public.

Specifically, the following discussions were held, following two large preliminary meetings - the first with representatives of technical and scientific groups; the second with representatives of national organizations of the consumer public:

a. Twice, conferences were held with each of the six vaccine manufacturers individually to discuss alternative proposals for distributing the

vaccine on a voluntary basis. These meetings resulted in a mutual understanding of the problem involved and enabled the Service and the manufacturers to jointly plan a system which was acceptable to all parties concerned.

b. The Secretary of the Department of Health, Education, and Welfare and the Surgeon General of the Public Health Service met with the Conference of State Governors to discuss the problems of equitable distribution of the vaccine, including the areas of Federal and State responsibility. Following this meeting, a Governors' Advisory Committee on Salk vaccine was appointed.

c. A meeting was held with the Governors' Advisory Committee for discussion of the plans being framed by the Department. General approval was indicated by the Committee, which agreed to poll all Governors with respect to certain questions.

d. Two meetings were held with the Executive Committee of the Association of State and Territorial Health Officers to discuss the merits of alternative plans for distribution and use of the vaccine. In these discussions, particular emphasis was given to the methodology and procedures which State health officers would follow in carrying out pertinent provisions of the plan.

e. The proposed plan was discussed with the Board of Trustees of the American Medical Association. The Association and other medical groups pledged their full support in carrying out the plan and the priority system.

f. Several elements of the plan were discussed with representatives of the pharmaceutical industry as a means of determining the plan's feasibility and obtaining suggestions for its improvement, particularly with regard to those provisions affecting retail druggists.

g. After development of the plan for distribution and use, it was discussed and cleared with the National Advisory Committee on Poliomyelitis Vaccine.

In all instances there was a high degree of cooperation and assistance from the groups participating in the planning.

Definition of Responsibilities of Public Health Service, State Agencies, and Manufacturers - Under the allocation system developed, it is the responsibility of the Federal government to arrange for the equitable apportioning of poliomyelitis vaccine among the States--in accordance with each State's population in the current nationally recommended priority group. With the concurrence of the groups noted above, each State is allocated its proportionate share of the vaccine supply periodically cleared and released by the Public Health Service.

The essential elements of the interstate distribution plan are as follows:

a. The National Advisory Committee on Poliomyelitis Vaccine from time to time recommends to the Department a specific age priority group to receive the vaccine.

b. Based on the number of persons in each State in the Federally recommended priority group, in relationship to the total number of such persons in the Nation, each State is allotted its proportionate share of each lot of vaccine released.

c. Each State advises the Public Health Service of the percentage of each allotment of vaccine which should be sold to public agencies and the percentage which should be sold in regular commercial channels to druggists and physicians.

d. Each manufacturer restricts the sale of vaccine to public agencies and to druggists and physicians to the percentage prescribed by each State.

e. Each manufacturer provides the appropriate State health department with copies of invoices showing vaccine sold so that the State will be able

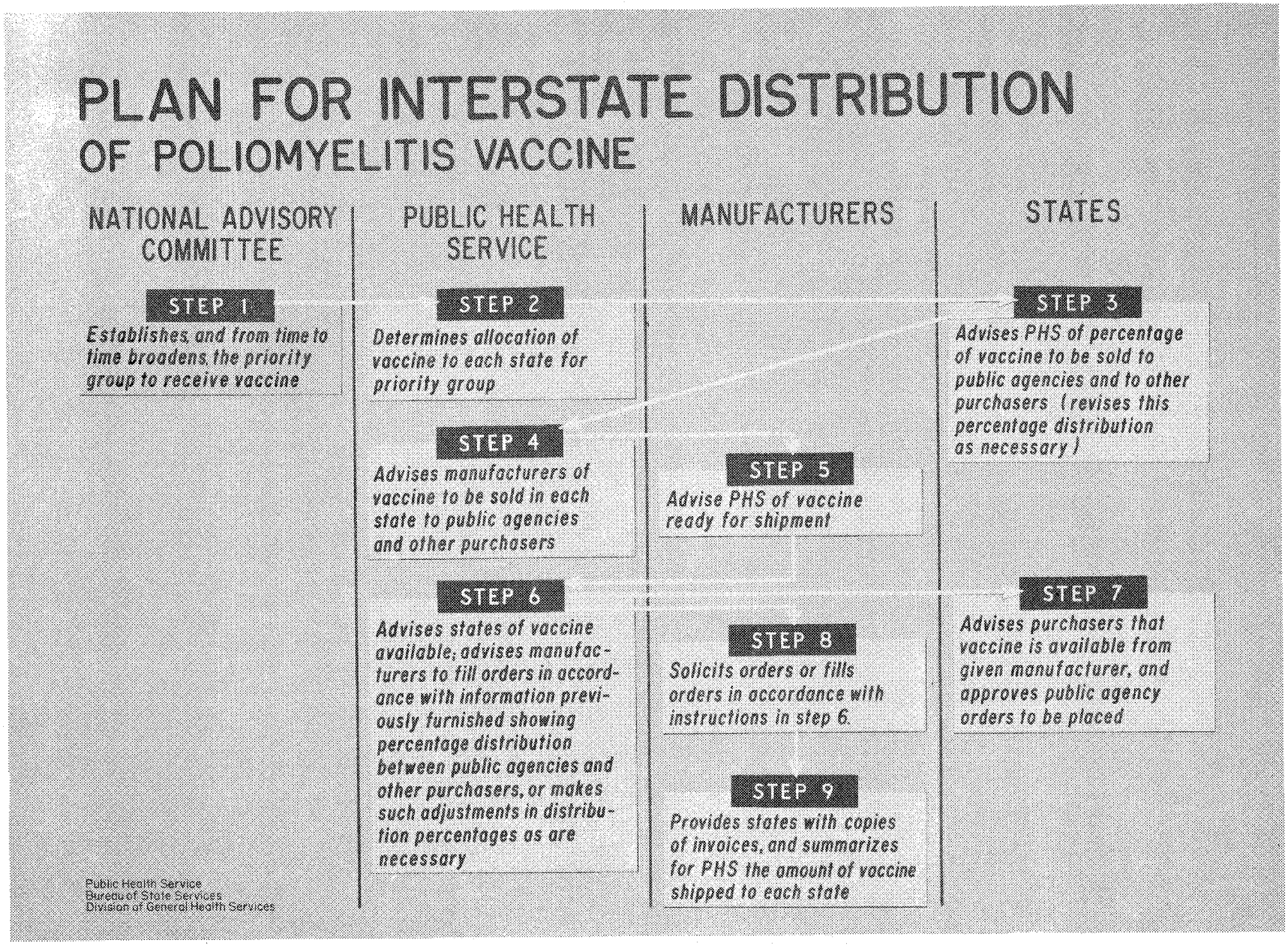
to detect and secure adjustments of inequities in intrastate distribution of the vaccine.

Chart 2 illustrates the manner in which the interstate distribution plan works.

Intrastate Plan for Distribution of Poliomyelitis Vaccine

Intrastate Plans. It was obvious that the effectiveness of the vaccine distribution would depend to a large extent upon the effectiveness of plans adopted by the State to control the intrastate distribution and use of the vaccine. The Public Health Service worked with the Executive Committee of the Association of State and Territorial Health Officers in developing suggested principles which might be used by the State in developing intrastate controls (12).

PLAN FOR INTERSTATE DISTRIBUTION OF POLIOMYELITIS VACCINE



Public Health Service
Bureau of State Services
Division of General Health Services

CHART 2

All States except Idaho have developed plans for the intrastate control of the distribution and use of the vaccine. Because the problems of distribution and use vary from State to State, each State's plan is tailored to meet its particular requirements. A summary of the salient features of such plans is given below:

a. All States and Territories, with the exception of the Canal Zone, Guam, and American Samoa, appointed an Advisory Committee. Although the membership of these committees varies from State to State, generally the groups most interested in the program, i.e., the medical association, public health officials, and the pharmaceutical association, are represented.

b. State health agencies report that, on the whole, excellent cooperation of the medical and pharmaceutical professions has been secured.

c. Allocation of vaccine within each State is based generally on the age priority group population of the local subdivisions. The amount of vaccine distributed to local subdivisions or other specific areas of the State is tabulated, and, when inequities occur, adjustments are made in allocating additional lots of publicly purchased vaccine. A number of States have also adjusted their initial allocations in accordance with demand, which varies widely from county to county. In order to meet the diverse needs, subsequent lots of vaccine are often distributed on the basis of requests rather than in proportion to the eligible population. In making these adjustments, State health agencies sometimes request that manufacturers increase or decrease the sale of vaccine in particular areas.

d. Most States report that the extent to which vaccine will be administered in public clinics and by private physicians is determined at the local level--usually by the county or city health department in cooperation with the county medical society. In counties without a

full-time health department, the local medical society, a special poliomyelitis committee, or other local group is utilized in coordinating the program.

e. The majority of States are furnishing some free vaccine to physicians, upon request, for use in their private practice.

Priorities. During the early months of the program--when demand for the vaccine far exceeded the supply--the National Advisory Committee recommended that its administration be restricted to children in the 5 through 9 age group. (See page 19.) On a Nationwide basis, this group was at greatest risk. The Federal age-group priorities are not binding upon the States so far as intrastate allocation and use of the vaccine is concerned. Nevertheless, once the vaccine had been allocated to the States on the basis of those age groups, with a few exceptions States and Territories followed the recommendation of the Committee, and established as the first priority group children aged 5 through 9.

By early October 1955, the vaccine supply was approaching fulfillment of the demand for two injections each to the 5 through 9 age group. Almost 24,000,000 cc. of vaccine had been released by the Public Health Service--enough to give two injections to three-fourths of the 16,000,000 children in this age category. In order to expedite prompt use of the vaccine, many States had recommended to the Service that the priority group be enlarged so that vaccinations might be extended to additional ages.

On October 12, the Secretary of the Department of Health, Education, and Welfare, acting upon the unanimous recommendation of the National Advisory Committee on Poliomyelitis Vaccine, broadened the priority group to receive poliomyelitis vaccine so that it could include persons ranging from birth through 14 years of age and pregnant women.

Because the vaccine supply was still short of total demand, the Secretary further recommended that each State initially extend its priority group to embrace no more than five additional years of age outside the original 5 through 9 age priority group, and, if so desired, to include pregnant women. This is to enable the States to move, in an orderly way, into lower or higher age groups, according to local incidence and severity of the disease.

As a result of the differences among the States in the age groups most susceptible to poliomyelitis, the broadened priority groups adopted by the States varied considerably. This variation is demonstrated in the following tabulation of current priority age groups:

Priority Age Group	Number of States & Territories
1 year and under - through 9 years	6
1 year and under - through 10 years	7
1 year and under - through 14 years	26
1 year and under - through 15-19 years	6
3 years - through 12 years	2
5 years - through 9 years	4
5 years - through 14 years	2

In addition, all States and Territories except 12 include pregnant women of all ages in their priority age group.

With the broadening of the Federal priority age group, the allocation of vaccine among the States will now be based on their need for vaccine to complete the vaccination of children under 15 years of age and pregnant women. This involves an addition of approximately $36\frac{1}{2}$ million persons to the priority group.

According to the State plans submitted to the Public Health Service, State health agencies and their Advisory Committees have been supported by State and local medical societies in obtaining conformance by private and clinic physicians to priority age groups established by the State. Moreover, the plans provide that physicians will maintain records of all children vaccinated. The information recorded usually includes name, address, and age of child and site

and date of vaccination. In most instances, this information is filed routinely with the State health agency--either in detail, or in summary. Where data are not filed in detail they are available for spot checking by the State agency, thus providing assurance of adherence to priorities in use of the vaccine.

Immunization Schedule. On December 7, 1955, a group of leading virologists, immunologists, epidemiologists, representatives of the medical and health professions, and of the National Foundation for Infantile Paralysis discussed the possibility--during the period of short supply--of giving one cc. of vaccine to all individuals in the most susceptible age groups before giving any more second or booster injections. This alternative immunization schedule was considered as a possible means of giving protection to more persons during the coming poliomyelitis season. The group concluded that there was not enough scientific evidence on the duration of immunity after a single injection to support a recommendation for a change in the present immunization schedule. The Public Health Service concurred in this recommendation.

Federal Assistance for Purchase of Vaccine

Poliomyelitis Vaccination Assistance Act of 1955. Recognizing the importance of rapidly protecting as many children as possible from poliomyelitis, the President in April stated his belief that Federal funds should be appropriated to assist in the vaccination program. The Secretary of the Department of Health, Education and Welfare submitted to the Congress a proposed Poliomyelitis Vaccination Assistance Act of 1955, which - with substantial amendments - was enacted. This Act became law on August 12. It provided for grants to the States to be expended by February 15, 1956. Congress has appropriated $30,000,000 to carry out the purposes of the Act. Of the total amount appropriated, $25,000,000 is available to the States for the purchase of vaccine only. The allotment formula is based on eligible population (unvaccinated children under 20 years of age and expectant mothers) and per capita income. The remaining $5,000,000 is available

to the States for purchase of vaccine or the cost of administering the poliomyelitis vaccination distribution program. No State matching is required for either portion of the allotment. The Public Health Service may furnish vaccine in lieu of cash to a State, if the State so requests.

Applications for participation under the Poliomyelitis Vaccination Assistance Act have been submitted and approved for all States and Territories, except Massachusetts.[3] Allotments totalling $29,313,147 are available to the States and Territories having approved applications, and $7,674,776 had been certified for payment as of December 31, 1955. The disparity between allotments and payments occurs because funds are paid only as needed to purchase vaccine which has been released. Thirty-five States plan to use all or a part of their allotment of the $5,000,000 for the purchase of vaccine.

Currently, the Public Health Service is purchasing vaccine for 22 States, upon their request. As of December 31, the Public Health Service had placed purchase orders with manufacturers for 3,939,624 cc. of vaccine for these States.

Some of the salient features of applications submitted under the PVA Act are given below:

a. All States agreed that vaccine purchased with Federal grant funds would be used only for the vaccination of children under the age of 20 and expectant mothers, and that records of name, age, and address of child and of place and date of vaccination would be maintained to substantiate this fact.

b. In describing the methods under which vaccinations will be made available, most States indicated that they would follow the traditional patterns of providing immunizations by using regular and special clinics, school clinics, and, upon request, distributing vaccine to physicians for use in their private practice.

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[3]Massachusetts, on the basis of a recent decision of its advisory committee, has now prepared a plan which will be received by the Public Health Service within a few days.

Of 48 States reporting on this specific item, 11 are using all publicly purchased vaccine in public clinics. Six States reported that all was being used by private physicians. In 18 States, more than 90 percent is being used in public clinics; in 23 - 70 percent or more; in 31 - 50 percent or more.

c. As required by the Act, all States and Territories agreed that no means test or other discrimination based on financial ability of individuals would be imposed to limit the eligibility of persons to receive vaccine provided through public agency programs, regardless of the source of funds used to purchase the vaccine.

d. In all States, the State health department was designated by the Governor as the single agency to administer the program.

General Health Funds Available for Poliomyelitis Activities. The "Assistance to States, General" appropriation for 1956 provided $4,500,000 to be available to the States for planning and operating a program for distribution and use of poliomyelitis vaccine. This amount was appropriated as a part of the General Health grant and was earmarked exclusively for poliomyelitis activities.

Plans for distribution and use of poliomyelitis vaccine (an integral part of the applications submitted under the Poliomyelitis Vaccination Assistance Act of 1955) have been submitted and approved for all States and Territories. The total amount of $4,500,000 has been allotted to the States and Territories. As of Dec. 31, $2,031,079 had been certified for payment.

Table 3 summarizes the current status of Federal funds appropriated for assistance to State poliomyelitis vaccination programs.

Table 3. - Disposition of Federal Funds Appropriated for Assistance to State Poliomyelitis Vaccination Programs, Fiscal Year 1956.

Authority	Appropriated	Allotted	Certified for Payment*	Balance Available
P.L. 410	$4,500,000	$4,500,000	$2,031,079	$2,468,921
P.L. 377 (Poliomyelitis Vaccination Assistance Act of 1955)	30,000,000	29,313,147	7,674,776	21,638,371

Enforcement of Federal Food, Drug, and Cosmetic Act

The Food and Drug Administration of the Department of Health, Education, and Welfare is responsible for ascertaining that poliomyelitis vaccine shipped into a State in normal drug channels remains in those channels and is sold at retail

* As of December 31, 1955.

level only to licensed physicians, or on their prescriptions. This involves inspection and examination of establishments and records to obtain information regarding manufacture, transportation, wholesaling, retailing, and use of the vaccine. On the basis of this information, violations of the Federal Food, Drug, and Cosmetic Act are determined, and, where indicated, appropriate regulatory action is instituted.

In carrying out its law enforcement program, the Food and Drug Administration has had the cooperation of industry. Manufacturers of the vaccine have furnished complete records of each batch distributed. Representative shipments have been selected for investigation on the basis of equitable coverage of each manufacturer, geographic area, and population concentration. The purpose is to determine whether the vaccine reaches the intended consignees in the invoiced quantity, and whether thereafter it is legally distributed.

To date, Food and Drug inspectors have visited 200 wholesale druggists, 4,900 retail pharmacies, 4,000 physicians, 400 hospitals, 100 health agencies, and 60 private homes in connection with the poliomyelitis vaccine program. Although a few instances of improper handling were discovered, there has been no problem of black marketing or illegal distribution. The Food and Drug Administration advised the Public Health Service of a few cases of possible use of vaccine outside the authorized age groups and failure to comply with the established distribution program. This information has been transmitted to the State health agencies concerned for appropriate action. Occasionally, stocks of out-dated vaccine and of stocks held without refrigeration were observed. These were also reported to the health authorities.

Practically all groups involved in the distribution of poliomyelitis vaccine have indicated a desire to make certain that the vaccine remains in legitimate channels. There has been no necessity for legal action.

Part III

CURRENT STATUS OF PROGRAM

Safety and Effectiveness

As explained in pages 7-13 of this report, epidemiologic observations throughout the country are providing a wealth of evidence which confirms the safety and potency of the Salk poliomyelitis vaccine. Although final data are not yet available, the reports accumulating clearly demonstrate the effectiveness of the vaccine as a preventive agent against paralytic poliomyelitis during the past season. For paralytic poliomyelitis, the rates are from two to more than five times greater among unvaccinated than among vaccinated individuals.

With respect to safety, experience with vaccine produced under the revised standards which have obtained since May 27, has been entirely satisfactory.

The Surgeon General has strongly urged that "Every available drop of the vaccine be used as expeditiously as possible by health agencies and private physicians to assure that the largest number of susceptible individuals are vaccinated before the next poliomyelitis season" (13).

Supply, Distribution, and Use of Poliomyelitis Vaccine

Supply. One of the most acute problems in the program to date has been the difficulty of forecasting future production and release of the vaccine. The large number of tests required to ensure safety of the vaccine, and the many scientific variables involved in the production and testing process, have made it impossible to estimate accurately the future production and release of vaccine. It is anticipated that early in 1956 the production and release of vaccine will become more stable, and future production will become more predictable.

There are approximately 65,000,000 persons in the age group 0 through 19 years or who are pregnant. To vaccinate this group of persons requires 195,000,000 cc. of vaccine. Up to December 31, about 30,000,000 cc. of vaccine had been released,

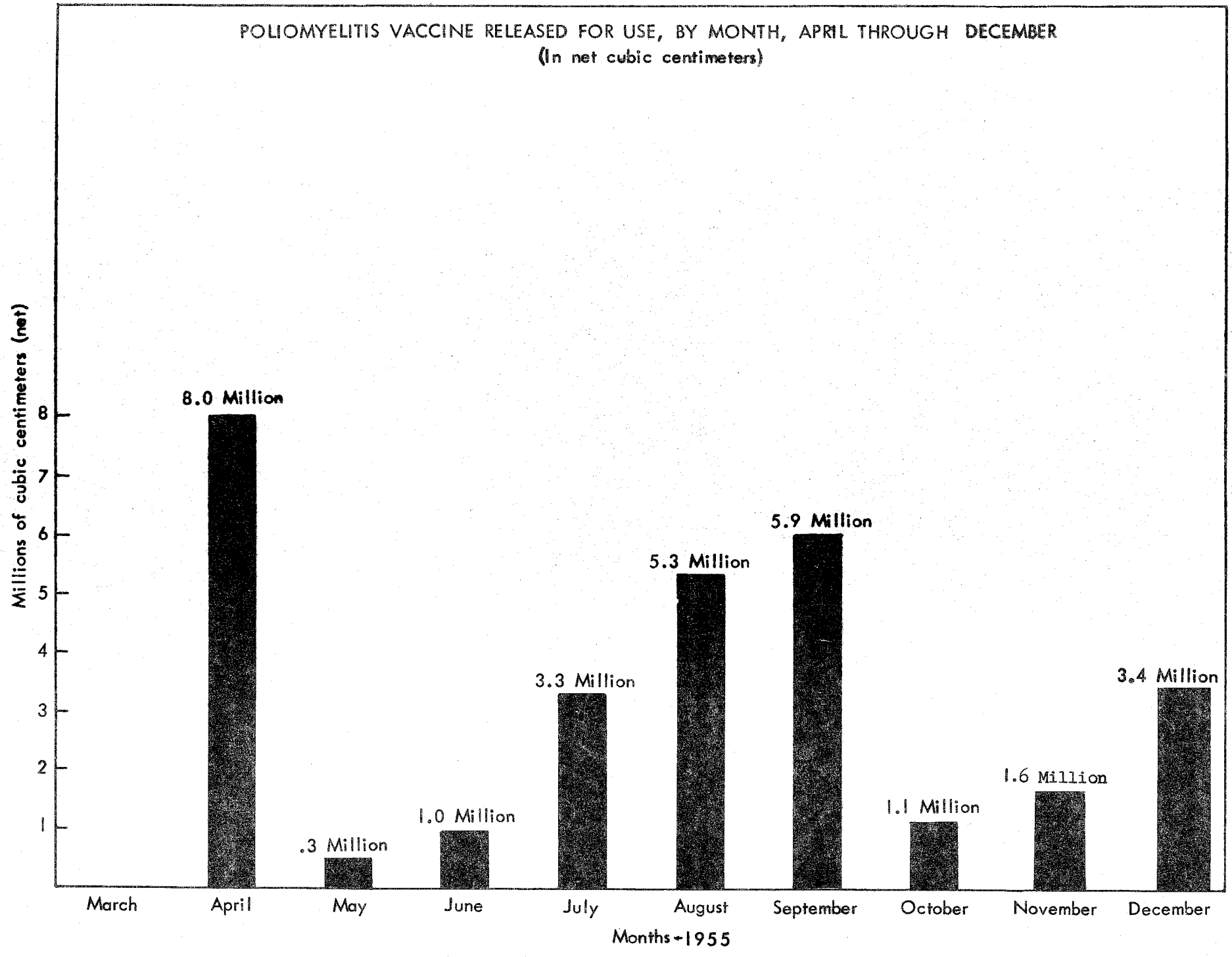
45 per cent of which went to the National Foundation for Infantile Paralysis for immunization of first and second grade children.

On July 30, 1955, vaccine was released for the first time under the interstate distribution plan. During August, 5.3 million cc. of vaccine were released, and 5.9 million cc. were released during September. In October and November, the quantity of vaccine released dropped sharply. In October, 1.1 million cc. were released; in November 1.6 million cc. were released. (See Chart 3.) Reduction in releases during these two months can be attributed largely to the major changes made last May in vaccine production and testing, and to the continuing refinements since then. By December, momentum had picked up, and the amount of vaccine released rose to 3.4 million cc. It is expected that from this point on, releases will be increasingly regular and larger.

Distribution. The mechanics of distributing vaccine on an interstate basis are now well understood by manufacturers and State health officers. As a result, this phase of the total problem presents few difficulties. The manufacturers have expressed general satisfaction with the way the distribution program has operated, and have stated that they believe all geographic areas have been given an equal opportunity to obtain vaccine.

Most State health officers have been, and are, making a determined effort to inform physicians, pharmacists, the general public and others concerned of the distribution problems within the State and the methods being followed by the State

POLIOMYELITIS VACCINE RELEASED FOR USE, BY MONTH, APRIL THROUGH DECEMBER
(In net cubic centimeters)



in administering the program. The degree to which State health officers are successful in this regard varies from State to State, but, in the main, the informational programs of the States appear to have been effective.

Of the first lots of vaccine released to the States under the distribution plan, about two-thirds was released for sale to druggists and physicians through local distribution channels. However, as funds became available to the States under the Poliomyelitis Vaccination Assistance Act of 1955, the quantity of vaccine released for sale to public agencies has increased. At the present time, more than 60 percent of the vaccine released is being reserved for sale to public agencies.

Use. Reports from manufacturers and State health officers reveal that, in most States, the demand for and sale of vaccine is heavy. However, because of local differences in interest, medical and public health resources, and plans of operation within the several States, there are wide local variations. In order to prevent accumulation of excess vaccine in some areas while there is a deficiency in others, State health agencies have maintained close intelligence over usage of the vaccine and promptly arranged for adjustment of supplies in order to obtain maximum value from the limited amounts available.

A few of the steps being taken to expedite use of the vaccine are cited here:

1. Original shipments were allotted to counties on a strict population basis; all subsequent shipments on a basis of local requests. Records are maintained by the State health agency of the vaccine allotted to each county. These records are compared with reports of numbers of injections and balance of vaccine on hand received monthly from each county. From such comparisons, requests of the counties for more vaccine can be evaluated and a flow of vaccine into the areas where the need is greatest is assured.

2. After several distributions had been made on an objective population basis, queries were sent out to local health officers asking:
   (a) "Have you more than enough vaccine for the needs of your jurisdiction, if so how much can you release?"
   (b) "Do you have less vaccine than you need for your program, if so how much do you need to complete it?"

   On the basis of these replies, vaccine is being transferred from areas where it is not currently being used to areas where the demands are great. On the next distribution, each local health officer will be asked how much vaccine will be needed in his area before it is shipped.
3. Allocations of publicly purchased vaccine are being increased in areas where sale of vaccine through normal commercial channels is lagging, and reduced in areas where greater quantities of commercial vaccine are being utilized. This has the effect of stimulating sales through commercial accounts.
4. The State Board of Health set up a vaccine exchange program through which physicians and druggists having too much short-dated vaccine could turn such vaccine over to their county health department where it would be promptly used before becoming outdated. The physician surrendering the vaccine received a memorandum receipt against which he could claim replacement as needed. Representatives of the drug manufacturers picked up surplus vaccine in the hands of physicians and druggists and redirected it into public channels where it was needed on the basis of immediate demand.

It is apparent from the reports received from State health departments that the States are maintaining a close surveillance over the vaccine distribution programs within their respective boundaries and that they have developed successful methods for obtaining rapid use of the vaccine.

In making these adjustments the State health agencies have enjoyed the wholehearted cooperation of the drug manufacturers, and have thus achieved the most effective use of vaccine available.

On a State-wide basis, the demand for and sale of vaccine has been brisk in most instances. In only five States (Idaho, Louisiana, Maine, Massachusetts, and Washington) have sales lagged sufficiently to require reallocation of vaccine to other States. With the recent approval of Idaho's State plan, replacement of vaccine temporarily withdrawn from this State was begun. The Massachusetts program, temporarily suspended pending more information regarding vaccine safety, has now been given a "green light" also and vaccine reallotted from this State will also be replaced as use there warrants.

Experience in the program to date has shown, as would be expected, that there is an interval of time that must elapse between the release of vaccine, the shipment of vaccine, and the use of vaccine. This interval results from a number of factors:

a. Necessary time required to place orders, verify orders, and make delivery.

b. Necessary time required to distribute vaccine from a central point in a State to the various localities where vaccine is to be used.

c. Necessary time required to accumulate enough vaccine in a State or local community to warrant publicizing and conducting clinics.

d. Necessary time required--after the amount of vaccine available in a local community is known--to schedule clinics, to publicize the clinic, to secure consent slips from parents, and to arrange for professional services.

e. Retaining of vaccine locally by health officers or private physicians to ensure that supplies will be available to give second injections to those children who receive their first injection.

The accumulation of sufficient quantities of vaccine to warrant scheduling of clinics and the retaining of vaccine for second injections have been of particular significance while vaccine has been in very short supply, since public agencies and physicians could not count on adequate supplies of vaccine being available to them on future dates.

Because of these factors, it cannot be expected that the number of injections of vaccine given on any date will equal the number of cc. of vaccine released or shipped on that same date. As supplies of vaccine become greater, more regular, and more predictable, it is reasonable to expect, on the basis of experience to date, that the interval between release of the vaccine and its use will be reduced.

The astuteness and flexibility with which States are operating their vaccination programs to meet specific local problems lead us to believe that every effort is being made to vaccinate as many children as possible between now and May and June, when a rush for vaccinations is anticipated.

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